

patterns confirmed that mesoderm is a source of *Edn1* signal. Gain- and loss-of-function approaches, the use of a specific *Ednra* inhibitor, and embryological experiments show that *Edn1/Ednra* signaling is required for neural crest development through a dual mechanism that controls neural crest specification and cell survival. The blocking of the apoptosis by a *Slug*-inducible construct in NC explants indicates that the control of NC specification by *Edn1/Ednra* signaling is independent from the control of cell survival. In addition, the epistatic analysis shows that *Ednra* is downstream *Msx1* and upstream *Sox9* and *Sox10* in the NC specification cascade. Our results provide insight on a new role of *Edn1/Ednra* cell signaling pathway during NC development.

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#### Program/Abstract # 115

##### Substrate selectivity by proprotein convertases

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Proprotein convertases (PCs) are a family of serine proteases important for cleavage of various substrates, including growth factors and morphogens during development and viral proteins during pathogenesis. There are seven PCs that have been identified in vertebrates—PC1, PC2, furin, PC4, PACE4, PC6, and PC7. In vivo evidence suggests that each of these PCs cleaves distinct, albeit in some cases overlapping, targets. However, targets have been difficult to identify because in vitro analyses have yielded little if any specificity; and moreover, mouse models in which PCs have been knocked out are too complex due to other PCs compensating and cleavage of multiple targets being disrupted. In order to combine the directness of in vitro analysis with in vivo relevance, I have developed an assay using biochemistry in *Xenopus* oocytes to identify in vivo targets of PCs. Specifically, I have used this assay to identify the PCs responsible for cleaving three candidate TGF $\beta$  family members—BMP4, Xnr2, and Activin<sub>BB</sub>. For the first time in vivo, I have direct biochemical evidence that BMP4 is cleaved by furin and PC6, Xnr2 is cleaved by furin and PACE4, and Activin<sub>BB</sub> is cleaved by furin. I will next use this assay to probe the question of what determines PC selectivity, as this has not been well characterized. Preliminary evidence suggests that sequences within the substrate prodomain may contribute to selectivity, so I have swapped prodomains between these three TGF $\beta$  family members and will determine which PCs can now cleave the chimeric constructs in vivo. These studies, once completed, will further our understanding of how PCs accomplish substrate selectivity.

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#### Program/Abstract # 116

##### Role of adherens junctions in regulating neurogenesis in the vertebrate central nervous system (CNS)

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Adherens junctions (AJs) are protein complexes that localize to apico-lateral regions of epithelial cells and maintain tissue integrity and cell polarity. In the newly formed neural tube, progenitor cells are interconnected by AJs and form an epithelial layer surrounding the brain ventricles, while neurons are loosely associated mesenchymal cells found in more basal regions of the neural tube. AJs are typically thought to function as cell fate determinants that are asymmetrically inherited by the progenitor cell upon cell division. Hence the retention of these junctional complexes in progenitor cells or their loss in differentiating neurons has conventionally been interpreted as a signal that regulates cell fate. However recent data suggest that these junctional complexes might in fact be maintained in newly born neurons, raising the possibility that the latter might signal back to progenitor cells to maintain them in an undifferentiated state. Here, using the zebrafish as a model system, we begin to analyze the pattern of inheritance of AJs in dividing progenitor cells and correlate the presence of AJ components with the fate of daughter cells. In addition, we address the in vivo role of AJs in the developing neural tube by characterizing several mutants in which these complexes are disrupted. Preliminary data suggest that AJs are required for regulating neuronal differentiation or/and cell division.

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#### Program/Abstract # 117

##### Subcellular distribution of endogenous Delta protein in the zebrafish embryo reveals a potential role for Notch in determining Delta endocytosis

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Mind bomb (Mib) mediated endocytosis of the Notch ligand, Delta, is essential for effective Notch signaling. In order to understand regulation of Delta endocytosis in zebrafish embryos, we examined the sub-cellular localization of endogenous Delta protein. In neural tissues, DeltaD protein was mainly localized in cytoplasmic puncta. In contrast, in mib mutant embryos most of the DeltaD was on the plasma membrane. This is consistent with the role of Mib in DeltaD endocytosis and suggests that Mib-mediated endocytosis normally results in most of the DeltaD retained in an intracellular compartment. However, surface expression of DeltaD could in part be due to exaggerated expression that results from loss of Notch signaling in mib mutants. To determine how exaggerated deltaD expression contributes to